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THE EVOLUTION AND USE OF THE ANIMAL DIGESTIVE FERMENTS IN MEDICINE.

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"Ever since the time 'ferments and ferment action' have been known," says Oppenheimer in his recent work on the subject, "their investigation has covered the whole field of inquiry in all branches of biology, because where there is life their manifestations play an important rôle. All the problems of animal and vegetable metabolism—in brief life—are in some way related to the province of the ferments."

Sir Michael Foster in his "Lane Lectures," 1901, declares: "The history of physiology can be regarded in no other light than as the heart or kernel of the history of medicine."

In attempting a review of the immense labors elucidating the nature of the ferments of digestion, we find ourselves confronted with a subject which, to present with the fulness it invites, would take us far beyond permissible limits. It is therefore necessary to attempt simply a brief, clear and authentic (in so far as possible) view of the genesis of the subject as it comes to and concerns us to-day in pharmacy and medicine.

Physiology, as a science, was evidently unknown to the ancients; and when the ignorance concerning human anatomy still existing at the beginning of the seventeenth century (Harvey discovered the circulation of the blood in 1628) is taken into consideration, physiology in general, as well as its application to digestion, must, at best, have been in its infancy at this period.

It is therefore remarkable that the Belgian chemist, Von Hel-

mont (1587–1644), should be credited with the statement that not the acids, but a definite body similar to those producing fermentation, was the vital principle of the stomach. Is this a modern construction of some of his writings, or is it one of those brilliant conceptions several centuries in advance of the times? As he termed all processes accompanied by the evolution of gases, even the effervescence of carbonates upon the addition of acids, "fermentation," our faith is somewhat shaken.

That the stomach played an important rôle in the digestion of food was no doubt evident to physicians of all times, but the value of the gastric juice and the existence of the secreting glands was first perceived by Borelli. (1608–1679.)

With the dawn of the scientific era and the application of scientific method in physiological investigations our knowledge of digestion expanded. In 1752 Reaumur published his investigations, carried out on a regurgitating buzzard or kite, and established the fact that digestion is independent of the mechanical power of the stomach; that a chemical change is produced in the food by the juices of the stomach, and that these latter have no action on vegetable food.

In 1772 Hunter noted the fact of post-mortem digestion, in which the stomach itself is digested and dissolved by its own juice. In 1777 we find Stevens applying Reaumur's method to a regurgitating man, but eliciting nothing new.

Then followed the classical researches of Spallanzani (1783), who by ingenious devices obtained from the living animal (birds and beasts) gastric juice quite free from extraneous matter. He was the first to clearly define the marked difference between peptic digestion and the phenomena of fermentation and putrefaction, and succeeded in demonstrating the potency of gastric juice outside of the body —in vitro. Inspired by Spallanzani's observations, Senebier, a surgeon of Geneva (Saint Evangele), suggested and employed gastric juice in surgery in the treatment of foul wounds, sores and cancers, etc., and his results being communicated to Jurine of Geneva, and Toggia of Turin, they (the former especially) made extended experiments in the application of gastric juice obtained from various animals—bullocks and sheep. They all observed that the gastric juice had the power "to remove all disagreeable smell from fœtid ulcers; to give them a clean appearance; to change the quantity and qual-

ity of the suppurated matter, and to obtain a speedy cicatrization." Carminati, a celebrated professor of medicine and surgery at Pavia, to whose notice these investigations were brought by Spallanzani, likewise used the gastric juice of animals as topical applications, and also used it internally in cases of indigestion, etc., with equally good results—the first recorded therapeutic use of a digestive secretion.

It is probably due to the absorbing interest manifested for the multitude of discoveries in all branches of science, more particularly in chemistry (by Scheele, Lavoisier, Gay Lussac, Berzelius and others), at the close of the eighteenth and the early part of the nineteenth century; probably also to the disturbed social and political conditions incidental to the Napoleonic wars, that the researches of Spallanzani did not become generally known. Then, again, the difficulty of the subject, the crudeness of existing methods, the want of exact instruments and appliances, may account for the conflicting opinions and theories, for the cessation of marked progress in the physiology of digestion, up to 1831. It was about this time (1828) that a discovery of the utmost importance in chemistry, the breaking down of the barrier between organic and inorganic chemistry, the destruction of the idea of the existence of a "life" force peculiar to organic bodies, viz., the synthesis of urea, was made by Wohler. This may well be conceived to have given a fresh impulse and promise to the isolation of some of the principles concerned in vital action, and thus to the study of the physiology of digestion, for the most important advances follow close on this time.

In 1824 by Prout—and independently by Thiedemann and Gmelin in 1826—free hydrochloric acid was found in gastric juice, and believed by the latter to be the digestive principle.

Luechs discovered, in 1831, the power of saliva to dissolve starch and convert it into reducing sugar; later Schwann, Mialhe and Cohnheim corroborated the statement and precipitated the active principle by various methods.

In 1834, the publication of the results of Beaumont's observations of natural digestion in the human stomach—in a case of a traumatic fistula—terminated the discussion regarding the existence, activity and acidity of gastric juice. Beaumont, however, advanced the theory of the combination of the juice with the food to form

"gastrites," and assumed the gastric juice to be the only digesting fluid of the body—an illustration of unfounded deductions leading to great error in association with important truths.

In the same year Eberle materially advanced our knowledge of digestion by successfully preparing active artificial gastric juice by scraping the mucus from the inner wall of the dead stomach and extracting the same with water and with dilute acids. He demonstrated that hydrochloric acid alone would not digest proteids and produce chymification. He however fell into the error of assuming that mucus itself was the active principle.

Eberle prepared similar infusions of other glands, particularly the pancreas, and was the first to note that it "liquefied gelatine, changed starch into sugar, and emulsified fat"—observations for which he does not seem to receive due credit.

Eberle apparently made no attempt to separate the ferment; but his method for preparing unlimited amounts of artificial gastric juice removed a great obstacle in the path of progress (scarcity of gastric juice, as well as contamination with other secretions, chyme, etc.) and paved the way for Schwann's brilliant researches in 1836. Apparently at the instigation of Johannes Müller, Schwann repeated Eberle's experiments, and this in so thorough and careful a manner that almost all of his observations and results hold true to-day. He found that the active principle was soluble in water and feeble hydrochloric and acetic acids; that acid was essential for its manifestations; that free acid alone had no solvent power on coagulated albumen; that the active principle was not in combination with acids; that an excess of acid destroys; that dilution does not weaken the activity if the acidity is maintained; that the action is a "contact action." He believed the ferment to be gradually destroyed during its action; that there is marked similarity between digestion and fermentation; but noted that no oxygen was consumed and no carbonic acid liberated during digestion; that the same causes arrest or destroy both, as heat, strong alcohol; that digestion requires acid, fermentation, oxygen; that in both, small quantities produce great changes. He tested the active principle in its behavior with acids, with metallic salts, with tannin; showed how it differentiated from albumen by not being precipitated with ferrocyanide of potash; from caseine by its failure to precipitate with ferrocyanide and acetic acid; and that it differs from "salivin" and

"ozmazome"—names given then to other forms of proteids. He attempted to ascertain its nature, whether simple or complex; noted the curdling action on the casein of milk and proved that this was not due to the acid; likewise studied its proteolytic power on muscular tissue and fibrin. Further showed that it was not mucin or a constituent of mucus, but secreted by the glands of the mucous membrane. He did not isolate the pure ferment (it has not been accomplished yet), but developed a method of purification by precipitation with mercury chloride and lead acetate, the metal being subsequently precipitated by hydrogen sulphide and removed by filtration. He was the first to ascribe a ferment nature to the active principle of the gastric juice, to which he gave the name pepsin.

In 1839 Wasmann—a pupil of Müller and Schwann—following the method of the latter, prepared a dry amorphous product by precipitating the filtrate, after removal of the metal, with alcohol, and drying the precipitate at low temperature.

Wasmann obtained a very potent product in this way from the pig stomach, extracting with water at 35–40° C.

He is stated by Frerich as having considered the active principle a combination of pepsin and hydrochloric acid.

The younger Burdach published, in 1841, the results of various experiments tending to show that acidulated infusions of many organs and tissues possess proteolytic powers. A glance at his results shows that this power was exceedingly weak.

In 1842, Blondlot in France, Bassow in Russia, succeeded in establishing gastric fistulæ in dogs; later on extended to the pancreas by Bernard, Heidenhain, etc. Blondlot in his treatise speaks of the nature of chyme, and in a rambling, incoherent manner of various fermentations, etc.

Lehmann, in 1842, treats of the manner of the proteolytic action of pepsin, considers it a protein of cellular origin and capable of transforming ingested albuminoids into substances susceptible of absorption. He credits Wasmann with regarding the granular matter in the glandular cells—the "cystoblastima" of Schwann—as either pepsin itself or the substance from which pepsin is formed.

In 1845 Bouchardat and Sandras published results obtained with the pancreatic juice of fowls, exhibiting great diastasic power. They subsequently continued their investigations on rabbits.

These authors are given credit for being the first to discover the

saccharifying power of the pancreas, although in 1833 Eberle found his artificial pancreatic juice to convert starch into sugar. Frerich gives the credit to Professor Valentin, of Bern, although Gamgee in his history now objects to this.

Bernard, in 1845, states that the whole function of the pancreas is its power to emulsify fat; this function was first noted by Eberle.

Frerich, in 1846, reviews the whole subject of digestive ferments, stating that the pancreatic juice changes starch to sugar, decomposes bile into insoluble substances for excretion, and, with the assistance of the bile, emulsifies fats. He argues in favor of an analogy between digestion and fermentation, combating the pepsin-hydrochloric acid and "contact" theories; assails Bernard for assuming that all of the various phenomena of digestion are produced by one and the same ferment, insisting upon the existence of independent ferments possessing specific powers, grouping them as digestive ferments.

In 1849 Bernard reports success in establishing pancreatic fistulæ in dogs, thereby opening up the field for accurate investigations of this gland. He failed to note its proteolytic function.

Bidder and Schmidt, in 1852, contribute a paper on the digestive fluids of dogs and cats, giving an analysis of gastric and pancreatic juices. With the latter they fail to obtain proteolytic action on coagulated egg albumen, but obtain marked action on starch. Their remarks on pepsin contain nothing noteworthy.

Although there is some dispute whether Eberle or Purkinji and Pappenheim should be given the priority of discovering the proteolytic power of the pancreas, Corvisart, in 1857, removed all doubt concerning the existence of the proteolytic power by careful systematic investigation. He pointed out that the activity of the juice varied with the time elapsed since feeding, and believed the failure of others to note this function of the gland due to killing the animal at the most unfavorable period of digestion, the most active being between the sixth and ninth hour after a full meal.

In 1858 Dr. Lionel Beale published a method of preparing pepsin by scraping the mucous membrane of the stomach and drying the viscid fluid so obtained on glass at a low temperature. He and Corvisart appear the first to suggest the use of "pepsin" in medicine.

Meissner, in 1859 and 1860, made an exhaustive study of both

peptic and pancreatic digestion, more particularly with a view to ascertaining the nature of the digestive products formed. Miahle was the first, according to Meissner, to use the term "albuminose" in reference to the products of proteid digestion, but the term as Miahle used it included all these products. Lehman, according to the same authority, proposed the term "peptone," and recognized different kinds of peptones, and described their character.

Meissner corroborated the results of Lehman, and discovered other intermediary products between albumen and peptone, experimenting on both raw and coagulated albumen, meat, etc.

Meissner likewise proved the correctness of Corvisart's results concerning the proteolytic power of the pancreas; but, strange to say, found it inert in aqueous and alkaline media and active only in acid medium.

He did not believe pepsin alone to be of any promise of therapeutic value, assuming it worthless unless acid was given at the same time. He therefore advocated the administration of peptone prepared outside the body with hydrochloric acid and pepsin, preferably from meat, as that from egg albumen was too bitter—the whole made more palatable by salt, spices, etc.—and gives a formula for preparing this peptone. He likewise suggested the use of the peptone solution as a nutritive enema.

Brucke, in 1859, published a very complicated method for preparing pepsin, said by him to yield a product quite free from adhering proteid matter. It is of scientific interest only, and probably seldom or never used now.

An interesting paper appeared in 1862, by Danilewsky, a pupil of Kuehne, on the active principles of natural and artificial pancreatic juice. It is written in a clear and definite manner, and seems to bring order into the confusion of views on the subject current at that time. His conclusions are that there are three distinct ferments present, acting respectively on starch, fibrin and fat; that two of these ferments can be isolated in a form of comparative purity, the fat-splitting ferment being probable; that the amylolytic ferment acts in acid, (?) alkaline and neutral media, the proteolytic in neutral and alkaline only; that the digestion of the coagulated fibrin is not due to putrefaction; that alkaline media is not favorable, excess of free alkali or free hydrochloric acid checking the action of fibrin. Further, that the proteolytic substance is not a pure albuminoid, but is a colloid substance.

Krassilinikow, a student of Brucke, first made use of dialysis in purifying pepsin in 1864.

Hoppe-Seyler, in 1864, published a comprehensive table, classifying the various forms of proteids, characterized by their solubility and by their precipitability with various neutral alkaline salts, as sodium chloride, magnesium sulphate, etc.

One of the earlier contributions on the pancreas, its ferments, the nature of its action on proteids, the cleavage products formed, etc., a subject that was made the special study of Kuehne and his pupils, appeared in 1867. Since then, up to 1880, numberless papers on the subject have appeared, and our present knowledge of this subject we owe largely to this investigator. Kuehne also gave the name trypsin to the proteolytic ferment, and introduced the term "enzymes" to designate this class of active principles, viz., the digestive ferments.

Von Wittich, in 1869, suggested the use of glycerin in extracting the pepsin, and this has since been employed extensively both in scientific research as well as in the manufacture of the digestive ferments and their preparations.

Scheffer, in 1872, published a method for preparing commercial pepsin by precipitation from an acid infusion of the stomach with common salt. He also stated that other neutral alkali salts, such as sodium sulphate and magnesium sulphate, could be used instead of common salt with good results. The action of saturated solutions of some of the neutral salts of the alkalies on different protein substances induced him to try their effect on pepsin.

In 1873 we find Ebstein and Grutzner demonstrating that pepsin does not exist as such in the stomach, but is rapidly formed from its progenitor—termed pepsinogen by these authors—by the gastric acid. Schwann and Wasmann seemed aware of this fact, but laid no stress on it. Langley, more recently, and Glaessner, during the past year, have given this subject careful study. Heidenhain discovered a zymogen, now called trypsinogen, in the pancreas in 1875.

Enabled by the great improvement in technic and by the introduction of antiseptic methods, Heidenhain, Klememsiwicz and Thiry during the seventies, Pawlow and his pupils during the nineties, observed the functions of the digestive glands under various conditions and influences in the living animal. Interesting and

instructive as these investigations are, we cannot dwell upon them here.

In 1883 Kuehne and Chittenden employed and advocated the use of ammonium sulphate as a superior precipitant of the albumoses, in separating these from true peptone.

Recent scientific inquiry seems directed chiefly to attempts to isolate the pure enzymes in the hope of ascertaining their chemical nature; careful examination of the cleavage products of proteids, produced by enzyme or by chemical action, to throw some light upon the structure of the proteids themselves. Schoumow, Simanowski (1894), Wroblewski (1895 and 1898), Pekelharing (1896), Friedenthal (1900) and Nencki and Sieber (1901) published investigations on the chemical nature of enzymes in support of their proteid nature.

Chittenden in connection with his various pupils, Osborne and Campbell, Hopkins, Kossel, Kutscher, Siegfried and others, have since Kuehne's time wrestled with the difficult problem of isolating and characterizing the multitude of forms of proteids, native and derived, but as yet the synthesis of albumen has not been accomplished.

Chittenden, chief among contemporaneous investigators in physiological chemistry, has made extended and varied experiments and researches, and has contributed voluminously to the literature on the subject. His experiments, in fact, are quite too numerous for reference. We cite these as especially pertinent: "Human saliva," "A comparison of natural and artificial gastric digestion," "Influence of peptones and certain inorganic salts on the diastasic action of saliva," "The relative formation of proteoses and peptone in gastric digestion."

It is also to be said that the studies of the illustrious Kuehne are likewise so voluminous that no adequately detailed mention of them can be made.

New methods of assaying the various preparations of digestive enzymes have been suggested by Kremel, Mett, Allen, etc.

The influence, deleterious and beneficial, of condiments, spices, beverages, antiseptics and medicinal agents upon the functions of digestive enzymes, received the attention of Chittenden, Stutzer, Buchner, Fraser, Mann, Mabery, Goldsmith, Roberts and others.

König. Bomer, Kjeldahl, Stutzer, Wiley, Mallett, developed

methods for ascertaining the composition and food value of the products of enzyme action, viz., the various albumoses and peptones of the market.

From the very first, we observe speculations upon the nature of the changes produced by digestion. Von Helmont believed it to be a fermentation; Eberle, chemical solution; Schwann, contact action differing from true fermentation; Frerich again speaks of it as fermentation; then Pasteur proved that fermentation was due to micro-organisms, and a distinction was made between organized and unorganized ferments, Kuehne suggesting the name enzyme for the latter.

Since Buchner's undoubted discovery in 1897 that alcoholic fermentation of sugar is produced by an enzyme—Zymase—which can be isolated from the yeast cell, the old theory that fermentations could only be produced by living cells, being inseparably associated with the life of these cells, has been shattered; and the thought that all true fermentations are caused by enzymes, and that the digestive processes, among others, should be classed as such is rapidly gaining credence.

The Zymase has not received complete chemical analysis, not having been prepared in sufficiently pure form. It appears to be very closely related to proteids.

Loew has described the enzymes as being very labile proteid substances, containing both aldehyde and amide groups. Oppenheimer denies that the enzymes themselves are labile, but capable of producing cleavage in other labile molecules, they themselves remaining unaltered.

The products of the digestion of food have naturally been the subject of scientific investigation related to the study of the ferments themselves, and to our subject; for the reason that foods increasingly enter into therapeutics both in the prevention and in the cure of disease. The main point of view from which it must be regarded in medicine is the physiological—that the prime function of digestion is the conversion of food of all classes into a soluble, assimilable and nutritive form.

The obstacles which we have encountered in the chemical investigation of the enzymes in a measure exist in relation to various proteids, native and derived, owing to their colloidal, non-volatile and readily decomposable nature. However, it is sufficient to state

that we have arrived in recent years at definite methods for the precipitation and separation of certain proteids, albumen, albumoses, peptones, etc., and the nitrogenous crystallizable, associated and derived principles of the food.

In the study of the derivatives of starch digestion similar difficulties are encountered in the separation of certain of the soluble carbohydrates, namely, the dextrins, but their color reactions are so marked as to afford reliable and well-known methods for distinguishing them. The crystalline nature of the sugars, the maltose and dextrose, has made their chemical constitution well known.

So we have authoritative methods for the analysis of food and food preparations. It is within the power of the analyst to distinguish between a preparation that is merely a stimulant and one that is, in the strictest sense, a complete nutritive; he is in a position to judge the degree of the change produced in the foods by digestion, and to form an opinion as to the relative assimilability of foods.

The coagulated albumen may, in its susceptibility to ferment action, be compared to gelatinized starch; the acid-albumen or syntonin, to soluble starch; proproteoses, to erythrodextrin; deuteroproteose, to achroodextrin; peptone, to maltose, and the more resistant antialbumen or dyspeptone, to cellulose.

The methods by which chemists distinguish these various soluble products in their various stages of solubility belong to the chemical side of the subject; their chief physiological significance is simply that as the digestion proceeds the substances become more soluble, more highly diffusible. Furthermore, chemical analysis as applied to these organic substances necessarily involves methods which, perfect for the chemist to distinguish their reactions and behavior, in themselves bring into play agencies never encountered in physiological conditions.

The influence of various and single food elements—sugars, albumen, gelatines, albumoses, peptones, etc.—have long been the object of study in the feeding of animals. These various substances have also been artificially introduced into the circulation and the effects observed.

When we come to trace the results of scientific research and experiment in the chemistry of digestion as taking practical form in pharmacy and medicine, we have to go back but a brief time,

especially if we restrict ourselves to that period when it can be said that the facts adduced concerning the nature and behavior and relations of the enzymes receive anything like general recognition, and their practical utility realized and applied.

Pepsin was first officially recognized in pharmacy by the French Codex of 1866, as pepsin medicinale, by the method originally suggested by Schwann and elaborated by Wasmann—the precipitation by lead acetate and evaporation of the purified solution of the pepsin, and incorporation with starch. Pepsin by this method first appeared in commerce from French sources.

In 1867 pepsin appears in the British Pharmacopœia, by the method originally suggested by Beale.

The first mention of any preparation of pepsin in the German Pharmacopœia is in 1872—"wine of pepsin" prepared from the stomach. The first preparation of pepsin appearing in the United States Pharmacopœia is pepsinum saccharatum, 1880; also the liquor pepsinæ, prepared from the saccharated pepsin. It was not until the Pharmacopœia of 1890, that an official standard was adopted for "pepsin," and the strength of saccharated pepsin prepared with this being increased six times over that of 1880. The U.S.P. defines no method of manufacture of pepsin. The special interest and significance of the pharmacopœial requirements of pepsin are in providing a commensurate standard of activity and practically complete solubility.

It is interesting here to note the digestive strength of these various official preparations of pepsin—the French forty times its weight of moist fibrin with lactic acid; the British one hundred times its weight; the U.S.P. pepsin three thousand, and the saccharated three hundred times its own weight of coagulated albumen. As for the pepsin of commerce, Boudault's is stated to convert four times its weight; Scheffer's saccharated digesting from ten to fifteen times its weight of coagulated egg-albumen in from five to six hours.

Scheffer's process and Scheffer's pepsin may justly be characterized as marking an epoch in the production of pepsin by a method admirably adapted for commerce. It had the great merit of employing reagents innocent in themselves and strongly antiseptic, and this is especially advantageous from the fact that the precipitate or magma which is collected is so strongly impregnated with the salt that either in the moist or pressed form it retains its properties under

the ordinary conditions of manufacture, without decomposition, until reduced to dryness.

It is to be noted in this connection that the sodium chloride and the other salts suggested by Scheffer threw out of solution a very large proportion of the soluble proteid bodies formed in the maceration of the stomach, or the stomach membrane, in the diluted hydrochloric acid at ordinary temperatures; the viscid solution thus formed containing the proteids very largely in the form of albumose, this giving an exceedingly copious, light, flocculent precipitate, which has the advantageous property of rising to the surface and of carrying the ferment embedded, so to speak, with the proteids in which it is associated.

By re-solution, clarification and re-precipitation, the product obtained could be purified to a considerable degree from the precipitant and associated proteids and salts of the gastric infusion, and a pepsin thus of great activity resulted. This Scheffer's "purified pepsin," however, did not come into general use in medicine, and was especially offered as a means of preparing saccharated.

Scheffer himself, although, as he remarked, confining himself specifically to the production of a pepsin, leaving its virtue to be established by physicians, nevertheless expressed the opinion that the "purified" (undiluted) pepsin might produce undesirable results. He considered the milk sugar desirable, therefore, in addition to its specific utility, as a means of reducing the pepsin to a pulverulent form, overcoming the obstacle inherent in the extremely tough and insoluble nature of the precipitated pepsin when reduced to dryness without some suitable absorbent.

Saccharated pepsin by the Scheffer process soon became very generally manufactured in commerce, but its very advantages, the facilities with which the raw material could be treated and the product obtained, may account for the appearance in commerce of pepsin which obviously could not have been produced by any means in accordance with Scheffer's methods, namely, the clarification of the acidulated solution, assay of the precipitated pepsin and incorporation of the diluent milk sugar to a definite standard of digestion test. Much saccharated pepsin of commerce was greatly deficient and feeble in action, so much so as to be of trifling value.

About ten years subsequent to the introduction of Scheffer's process there appeared a method, patented by Jensen, based upon the

fact long before recognized, as we have seen, that the stomach was capable of self-digestion, and thus the tissue of the whole stomach or the mucous membrane converted into a soluble form. This product when dried, therefore, contained the ferment in association with the peptones produced by its action. It is at this time unnecessary to state that the products of peptic action—the peptonized proteids—possess no digestive action (although at one time there appeared to be some impression of this current) and their hygroscopic nature distinctly unfits them as a vehicle or basis for commercial pepsin if associated in any large degree with the ferment.

It may be said that all pepsins are produced by processes embodying principles which have been developed by scientific research and experiment; at present, in brief, the infusion of the stomach by such methods as to obtain the ferment in solution as free as possible from associated proteids, or else by heat to convert the paptic glands into complete solution, and the precipitation of the enzyme from this solution by such well-known reagents as sodium chloride, sodium sulphate, magnesium sulphate, etc., and purification by various methods—dialysis, etc.

In these processes, advantage is taken of the fact that by infusion of the gland with heat, in acidulated solution, the whole tissue can not only be converted into solution, but carried forward to such a point as to yield a considerable proportion of peptone, this not being precipitable by the reagents mentioned; so that by this means the pepsin as precipitated is at the outset of a much higher activity than that associated, as already described, with a large amount of albumoses.

During this time no progress in the utilization of the pancreas ferments at all comparable to that in pepsin had been made, very evidently for the reason that scientific observations concerning the varied nature and action of the pancreas enzymes had either escaped attention or failed of appreciation. "Pancreatine" seems to have been made by methods almost identical with the "salt process" for pepsin, ignoring the fact that the pancreatic ferments are soluble in salt even in concentrated solutions—not precipitable by salt. Scheffer criticized this method, for he proved sodium chloride incapable of precipitating pancreatin.

In spite of the fact, then, that the pancreatic ferments had been shown to possess great energy in the conversion of starch and of

albuminoids, practical attention had been chiefly directed to the pancreas function of digesting fat, and even in this respect the pancreatine being defectively prepared (and saccharated) its value was practically negative.

Pancreatine was first officially recognized in the U.S.P. in 1890, and about this time the National Formulary recognized it with a method for its manufacture and adopted the U.S.P. standard as to its proteolytic power, especially relating to its practical use in the peptonization of milk.

"Pancreatine," as officially recognized by the U.S.P., is defined as a mixture of the enzymes of the pancreas gland, digesting albuminoids and converting starch into sugar.

Pavy, in 1867, suggested the first preparation of an artificially digested food, obtained from meat and preserved in a fluid form.

Roberts, in his Lumleian Lectures of 1880, demonstrated the adaptability and potency of the pancreas ferments for the peptonization of foods for the sick, especially the susceptibility of milk as well as farinaceous foods to artificial pancreatic digestion. He adduced numerous experiments as to the behavior of these ferments of practical significance, and suggested methods for preparing pharmaceutical preparations of them, discussing and illuminating the whole subject in this series of brilliant and practical lectures. It was he, it appears, who brought into use the word "peptonized" as a convenient term for the description of artificially digested foods.

The pancreatic ferments had been previously utilized in a very primitive and extemporaneous manner; for instance, treating meat by direct incorporation with the fresh gland, especially for nutritive enemata; "pancreatized" fats, in a similar manner, and pancreatic emulsions were also introduced into pharmacy, resulting from the treatment of fat by direct maceration with the fresh gland pulp.

(*To be continued.*)

FILTRATION OF DRINKING WATER.

By William G. Toplis.

The need of water purification begins immediately after its delivery by the mighty distillery of Nature.

Its contamination is commonly incident with its delivery, while its purification often follows closely by the operation of natural

laws; yet the great mass remains a source of the utmost solicitude so far as the health of communities is concerned. The impurities in water may be separated into two principal divisions, namely, Inorganic and Organic. That consisting of mineral substances, such as salts of K, Na, Ca, Ba, Mg, as may be dissolved by the water in its passage through the earth, is of the first class, and from a hygienic point of view is not of a particularly harmful character, though from a technical point of view it presents considerations of most serious importance.

In the second class is embraced every substance produced during the life-processes of plants and animals. It is to this source of contamination that our attention is most earnestly directed for the purpose of providing a wholesome and economical water-supply. To this kind of contamination is chargeable all of the diseases peculiar to drinking water. It must be plainly understood that disease is not necessarily due to the simple presence of organic matter, but such material invariably decays, and it is this change that causes the trouble by enabling pathogenic organisms to prolong their existence.

From the beginning of time Nature has rid herself of all dead organized bodies in but one way, decay, brought about by the growth of bacteria at the expense of the dead matter. These minute vegetable organisms, either by their mechanical presence or through their excretory products, are responsible for all water-borne diseases.

With such facts in mind, then, it is but natural that effort is being constantly put forth to remove from our water-supplies not only the bacteria, but the pabulum for their existence—the organic matter.

Nature has pointed unerringly the way. Springs have long been held in popular esteem as the source of pure drinking water, and not without good reason, for in the majority of cases springs sustain this reputation after chemical and biological examination. It has long been known that impure water percolated through a deep bed of sand issues greatly improved in chemical character, but the precise nature of the changes were not thoroughly understood until Koch's revelation made possible the isolation and study of individual species of bacteria. Art seeks to copy the changes so long carried out in springs, but with the precise care of scientific exactness instead of the haphazard of chance, as in

springs. The sand filter, therefore, means the most exacting, painstaking care to establish the proper conditions, together with the wise application of much chemical, bacteriological, and engineering knowledge. The container is commonly built of concrete, though masonry and puddled clay embankments are not infrequently used. The bottom of the container is carefully graded so that drainage will be equal from every part. The underdrains are given like careful attention for the same reason, and are built of broken stone or large gravel measuring 2 to 3 inches on 3 diameters. It is spread in a layer 6 to 8 inches deep; on top of this is spread several inches of smaller gravel then finer, until we have a bed 12 to 16 inches in thickness. Upon this is placed 4 feet of fine sand, exercising care to pack it evenly, and avoiding holes and ways. The chemical character of the sand and gravel must be carefully looked into, as it is important to avoid carbonates and sulphates of the second group. Much carbonic acid is formed during the operation of the filter, and this in solution has the property of dissolving carbonates of calcium magnesium, barium, strontium, creating increased temporary hardness, while any sulphate of calcium would materially add to the permanent hardness. The best material for the purpose is a sharp silicious sand. Having constructed the filter it is filled by introducing water at the bottom to avoid disarranging sand by escaping air. The filtration is at once begun, and bacteriological and chemical samples of water are regularly collected from the effluent and likewise from the applied water. At first there is but little difference in the character of the water, either bacteriologically or chemically. After a few days a comparison of the bacteriological counts on the raw water with those of the effluent will show a very marked increase of bacteria in the effluent over that of the applied water; this increase will steadily rise until after a variable period of time, usually two weeks, the counts rapidly diminish until they become less than one per cent. of the number in the applied water. At the same time a comparison of the chemical analyses of the effluent and applied water will show in the effluent greatly decreased free and albuminoid ammonia, practically no nitrites, and greatly increased nitrates. The operation during this period of time is known as the ripening of the filter. It embraces many complex changes of absorbing interest, and copies with scientific exactness the example which

nature carries out in springs under the most favorable conditions. For convenience of illustration, we may assume that the bulk of organic matter is embraced within the elements C, H, O, N. No matter how complex the molecules may be, the matter is ultimately broken down into the most simple compounds of the elements, namely, C into CO_2; H and O into water, and the N into nitric acid or salts of the same. This is all brought about through the functioning of those minute vegetable cells called bacteria, not instantly, but progressively; not necessarily all in one operation, but in consecutive changes, proceeding orderly and with deliberation until that which was organic and perhaps toxic becomes the most simple inorganic compounds of the elements, quite harmless and ready food for plant assimilation. This is all carried out in a slow sand filter, and the object is to cultivate rather than destroy bacteria. The sand is not the filter, the sand is simply the bones upon which the filter grows. Surrounding each individual bacterium, under the microscope may be seen a gelatinous envelope, when many bacteria are joined together in mass; this envelope may be seen collectively without a lens, forming a jelly-like mass and is then called a Zoogloea. In a sand filter this Zoogloea attaches to and covers completely each grain of sand in the filter. The grains form fine avenues through which the water is compelled to pass. The bacteria line these avenues. The water carrying its organic content brings it as food for the bacteria in the Zoogloea. As the water passes along, it is gradually relieved of its organic matter, because it is digested by the bacteria, and in its place bears away the products of the decomposition. Sublime in its beautiful simplicity! We have chemical and biological proof of each change. Those just mentioned are indicators of every step—C into CO_2; H and O into water, N into nitric acid and its compounds; but the proper conditions must be maintained, and perhaps the most important factor, aside from the bacteria, in the operation of the filter, is oxygen. Without this element the particular kinds of bacteria necessary for water-purification cannot perform their function. The oxygen must be in solution and carried along with the water into the filter, where it is utilized in the oxidation changes.

Winogradsky has shown that nitrifying or oxidizing bacteria grow upon media altogether inorganic. No less than three separate and distinct classes of organisms are concerned in the transition of nitrogenous organic matter to the inorganic state, as follows:

It is broken down into ammonia—as the first change by one class of organisms, and here becomes truly inorganic. The second step is one of oxidation, and the ammonia becomes nitrous acid through the agency of another entirely separate organism quite different from the first. In the third and final step, the oxidation is completed by another organism entirely distinct from the other two. Here the nitrous acid becomes nitric acid, which unites with any base at hand, and is delivered as such in the effluent. This is why our filter, working under favorable conditions, shows neither free nor albuminoid ammonia, but does return the equivalent in nitrates that an ammonia determination on the raw water would call for. As before stated, the proper conditions must be preserved, and one of these is the element of time; how rapidly may we pass the water through the sand as an economical proposition? As might be predicted, the character of these changes would require a slow rate of flow; therefore, filtration must be restrained or controlled and maintained at a uniform rate, notwithstanding a constantly diminishing filtering capacity due to clogging. This is accomplished in several ways by automatic devices. It is not safe to carry the filtering rate much beyond 3,000,000 gallons per acre per twenty-four hours. This has been found by actual working conditions to be the safe limit, so far as bacteriological and chemical conditions are concerned. A 3,000,000-gallon rate is equivalent to filtering 10 vertical feet of water over the entire area of filter in twenty-four hours. The problems met with in water purification seem to change with each source of supply, and so variable are they that no municipality would undertake the erection of a filtration plant without exhaustive study of the conditions covering practically a whole year. In some waters, color is the objection; in others, taste is complained of, while turbidity and sewage, with every imaginable combination of all the faults, is commonly found.

The principal problem encountered by the city of Philadelphia in its effort to purify the water is that of turbidity. True, we have sewage contamination, odors, tastes, etc., but they readily disappear under treatment. The turbidity, however, gives trouble, particularly at times of freshet, when the suspended matter may rise to 200 or 300 parts per million. This requires frequent scraping of the filter, resulting in loss of water and cost for attention. Under ordinary working conditions, with water carrying less than 40 parts per

million, the filter should not require scraping more than thirteen to fifteen times per year, but in times of freshet I have seen the experimental filters shut down and scraped once a week. This condition is exceptional, however. After scraping, the bacterial counts are high, so the water is run to waste for a period. My observation on this point was that forty-eight hours usually elapsed before the counts returned to the normal. The depth of water covering the filter is about four feet; this head forces the water through the sand. As the deposits accumulate there is diminished flow, gradually decreasing until the pressure is insufficient to deliver the 3,000,000-gallon rate, then the filter is shut down, drained and scraped.

The operation of scraping the filter consists of removing about ½ inch in depth of sand from the surface, together with the deposit of mud, etc., after which the surface is raked even and filtration proceeds as before. At the end of a year the total amount of scrapings is washed, loss made up, and returned to the filter in one operation.

In order to be sure that there are neither holes nor ways through the filter, an ingenious procedure is adopted as follows: Large quantities of a culture of Bacillus Prodigiosus are applied to the surface of the filter at regular intervals of half an hour each for a period of twenty-four hours. Millions of these organisms are introduced at each application. Test samples of the effluent are taken every fifteen minutes during the time of the trial. Plates are made of each sample and counted. The Bacillus Prodigiosus grows best upon agar-agar producing a bright red colony distinguished at a glance from the ordinary water bacteria. If there are any ways or openings in the filter the bacilli are sure to be found in the effluent. When the test was applied to this city's experimental filters we found but two plates showing red colonies out of several hundred trials, and it is just possible that these were accidental contaminations, proving conclusively the excellent construction of those beds.

In order to have the results of all bacteriological investigations comparable, it is absolutely necessary that the methods of manipulations be uniform. One most important stride in this direction was made by Fuller when he demonstrated that the medium most suitable for cultivation of bacteria for water work is that composed of gelatin 10 per cent., peptone 1 per cent., salt ½ per cent., dissolved in meat infusion representing the soluble portion of 500 grammes of

lean beef to a litre of water, the finished product having an acidity of 15 degrees. This means that a litre of such medium would require the addition of 15 c.c. of normal sodium hydrate solution to bring it to the phenolphtalein neutral point. It has been repeatedly demonstrated that this medium gives larger counts than the same material made more acid or more alkaline, showing the very marked influence that the degree of acidity exerts upon the development of the bacteria under examination. This medium is the one now used almost universally by water analysts.

The special apparatus used in quantitative bacteriological investigation is quite simple, consisting essentially of test-tubes and petri dishes. The petri dish is simply a circular glass vessel about four inches in diameter, with raised edge from three-eighths to one-half inch high. Two of these make a complete dish, the upper one fitting loosely over the lower. There are other pieces of apparatus, but those named are most in evidence.

Absolute sterility of media and apparatus is the only condition under which this work can be successfully carried out. To make a plate, the sterilized glass dish is set upon the level table; a tube of the gelatin medium, previously described, containing about 7 c.c., is fused by gentle heat, and when cooled to about blood temperature, a measured quantity of the water to be examined is introduced from a sterilized graduated pipette. The test-tube is shaken to thoroughly incorporate the water with the medium, which is then poured into the petri dish and immediately covered. After it has solidified it is placed in the incubator, where it remains for a period of forty-eight hours at a uniform temperature of 20° C., being the most favorable temperature for the cultivation of water bacteria. This period of incubation is adopted, because it not only indicates the condition as well as a longer time would do, but gives a more speedy notification of any change in the filters. Counting is done with the aid of a simple lens, and refers not to the number of bacteria on the plate, but to the number of colonies. Each colony is supposed to be the progeny of one original bacterium, and the count gives the relative number of bacteria in the water at the time of plating. Determination of species is unnecessary as a routine procedure, though frequent search is made for the Bacillus Coli Communis, as this organism is invariably present in sewage and serves as an indicator of its presence in the water-supply.

Chemical considerations require so much time for their description that I shall simply be content with naming over such processes as have been found most satisfactory at the Testing Station, Philadelphia. For this information I am indebted to Dr. George E. Thomas, the chemist in charge of this branch of the work.

For Color, Hazen's Platinum Cobalt Standard, described by Leffman.

For Turbidity, Whipple and Jackson, Mt. Prospect Laboratory, Brooklyn.

For Solids, 100 c.c., evaporate to dryness, with loss on ignition.

Suspended matter, collected on filter of asbestos, operating with a litre of water.

The two ammonias collect six tubes from each distillate for Nesslerization. The peculiar clouding of the distillate noticed at times on addition of Nessler Solution may be corrected by addition of mercuric chloride to Nessler Solution.

Nitrites.—Alpha naphthylamine hydrochloride and sulphanilic acid.

Nitrates.—Reduction by aluminum foil and direct Nesslerization of the ammonia.

Oxygen Consumed.—Potassium permanganate and oxalic acid.

1 c.c. potassium permanganate sol. = ·0001 gm. O.

Chlorine.—Titrate with nitrate silver, potassium bichromate as indicator; using yellow light gives sharper indication of end reaction.

Alkalinity.—Hehner's method, using $\frac{N}{50}$ H_2SO_4, described by Leffman.

Total hardness.—Soap method.

Oxygen dissolved.—Winkler's method in Sutton.

CO_2.—Seyler's method — $\frac{N}{50}$ Na_2CO_3, using phenolphtalein as an indicator, described in a recent issue of the *Journal of the American Chemical Society*.

SEIDLITZ POWDERS.

By Rolland H. French.

This paper is to be regarded as the result of an effort on the part of the writer to simplify the seemingly complicated and impracticable methods which have been set forth by previous investigators of the

subject, and, if possible, present a method of analysis which it would be practicable for the average pharmacist to carry out.

The most able effort on the subject which has come to the writer's notice is a paper by Joseph Huntington, which was published in the AMERICAN JOURNAL OF PHARMACY, 1900, p. 461, and reprinted in a number of other pharmaceutical journals.

In this the U.S.P. method of titration with potassium hydrate volumetric solution was used for tartaric acid. An indistinct end reaction is here encountered, unless carried out in hot solution, on account of a precipitate of potassium bitartrate.

The method for the estimation of the Seidlitz mixture consists in first estimating the sodium bicarbonate by adding an excess of sulphuric acid volumetric solution and titrating back with potassium hydrate volumetric solution. Second, another portion of the Seidlitz mixture is ignited, taken up with water, and titrated as in the previous case. The amount of solution required for the sodium bicarbonate alone is then subtracted, the remainder representing the Rochelle salt.

This method gave 31·44 per cent. sodium bicarbonate and 85·86 per cent. Rochelle salt, making a total of 117·3 per cent.

The 17·3 per cent., which this runs high, was accounted for from the fact that the work had been done in a warm room, which had caused a loss of moisture. No experiments were made, however, to prove the latter theory.

As can be seen, the working of this method is not at all satisfactory, and the inaccuracy of the final result does not justify the effort required.

The experiments which the writer has carried out on the subject will here be described and the conclusions reached noted.

A series of experiments were carried out with chemically pure salts to ascertain the possibilities and to afford a means of comparison for the work on the samples to follow.

Sodium hydrate volumetric solution was used for the titration of the tartaric acid, the precipitation thus being avoided, and perfectly satisfactory results being obtained in the cold.

Experiments were then made with the ingredients of Seidlitz mixture to ascertain the effect of exposure under various conditions. Quantities of Rochelle salt and sodium bicarbonate, corresponding to the weights given by the U.S.P. for one powder, also

a portion of Seidlitz mixture, all made from the C.P. salts, were exposed under ordinary conditions, that is, in a room ranging from 18° to 22° C., and their weight taken every two or three days during the course of four weeks. They were then placed in a room decidedly warmer than the average, ranging from 28° to 33° C., and the weights taken as in the former case. In both cases it was found that the condition of the weather had a good deal to do with the weights.

The characteristic results obtained by these experiments are best shown by a table, as follows:

Substance Taken and Weight in Grammes.	Temperature 18° to 22° C.			Temperature 28° to 33° C.		
	Weather and Date.	Loss in Grammes.	Per Cent. of Loss.	Weather and Date.	Loss in Grammes.	Per Cent. of Loss.
	Nov. 3, 1900, Started Experiment.			1901.		
Rochelle salt, 8,000.	Nov. 27th wet.	·002	·025	Jan. 3d wet.	·009	·112
	Dec. 9th dry.	·007	·087	" 10th dry.	·0115	·143
	" 15th wet.	·000	—	" 12th wet.	·008	·100
Sodium Bicarbonate, 2·600	Nov. 27th wet.	·004	·15	Jan. 3d wet.	·004	·15
	Dec. 9th dry.	·009	·34	" 10th dry.	·012	·46
	" 15th wet.	·0025	·09	" 12th wet.	·005	·19
Seidlitz Mixture, 10·333	Nov. 3d wet.	·065	·63	Jan. 3d wet.	·104	1·006
	Dec. 9th dry.	·099	·95	" 10th dry.	·145	1·403
	" 15th wet.	·092	·89	" 12th wet.	·127	1·229

Rochelle salt contains 25.52 per cent. water of crystallization. To determine the loss sustained by heating to various temperatures a portion was heated in an air bath:

At 100° the loss was 23·43 per cent.

At 130°–135° the loss was 24·19 per cent.

Above 135° decomposition commenced, showing it to be impossible to separate the last trace of water without decomposition.

Following these experiments, investigation was made upon six samples, all of which were collected without discrimination from reputable houses.

All were subjected to the qualitative tests of the U.S.P., after

which the quantitative work was taken up; the white powders or the tartaric acid were first examined, followed by the blue or the Seidlitz mixture.

Quantitative Tests.—The volumetric solutions used for these tests were:

Sodium hydrate, of which 1 c.c. = { ·05633 grammes NaOH ; ·01055 " $H_2C_4H_4O_6$

Sulphuric acid, of which 1 c.c. = { ·009327 grammes H_2SO_4 ; ·004184 " CO_2 ; ·2684 " $KNaC_4H_4O_6$

The tartaric acid was titrated with sodium hydrate volumetric solution, phenolphtalein as indicator, as mentioned in experiments, the calculation being made in the regular way.

The Seidlitz Mixture was analyzed by first estimating the sodium bicarbonate by a carbon-dioxide determination, then the Rochelle salt by ignition and titration.

This method will be best understood by carrying through an example, thus:

If 1·722 grammes of Seidlitz mixture be placed in a carbon-dioxide apparatus and a slight excess of hydrochloric acid used for decomposition, it will yield 0·225 grammes of carbon-dioxide gas. The amount of sodium bicarbonate is then calculated from this weight of CO_2 as follows:

(CO_2 43·85) : ($NaHCO_3$ 83·85) : : ·225 : ·42985 grammes of $NaHCO_3$,

then,

1·722 : ·42985 : : 100 : 24·96 per cent. of $NaHCO_3$.

For the Rochelle salt estimation another portion of 1·722 grammes is taken and ignited carefully in a small crucible to entire carbonization. This ignited mass is then taken up with water, all of the washings being carefully collected. This solution now contains the carbonates from the Rochelle salt, also that from the sodium bicarbonate. This solution is titrated directly with the sulphuric acid volumetric solution, using methyl orange as indicator. The solution of carbonates required 74·75 c.c. of the sulphuric acid solution.

From this must be deducted the number of c.c. required for the carbonate from the sodium bicarbonate in order to determine the

exact amount required by the Rochelle salt. This may be calculated directly from the CO_2 in the previous determination, but it must be remembered that one-half of the CO_2 from the bicarbonate has been driven off during its conversion into bicarbonate by ignition. Therefore, one-half of the CO_2 yielded by the bicarbonate must be used for determining the sulphuric acid required for the carbonate yielded from it.

This is shown by the following reactions:

$$2NaHCO_3 + \text{heat} = Na_2CO_3 + H_2O + CO_2$$
$$2NaHCO_3 + H_2SO_4 = Na_2SO_4 + H_2O + CO_2$$
$$Na_2CO_3 + H_2SO_4 = Na_2SO_4 + H_2O + CO_2$$

The calculation would be thus:

$$(\tfrac{1}{2} \cdot 225) \div \cdot 004184 = 26 \cdot 8 \text{ c.c. } H_2SO_4 \text{ V.S.}$$

Then 74·75 c.c. required for the entire carbonates less 26·8 c.c. required for the carbonate from the bicarbonate, leaves 47·95 c.c. required for the Rochelle salt.

The Rochelle salt is then ascertained thus:

$$47 \cdot 95 \times \cdot 2684 = 1 \cdot 28697 \text{ grammes Rochelle salt found.}$$

Then,

$$1 \cdot 722 : 1 \cdot 28697 :: 100 : 74 \cdot 731 \text{ per cent. Rochelle salt.}$$

The six samples were all examined and analyzed by the methods just described, with the results shown in the following table. The U.S.P. weights and theoretical per cent. are also given to enable comparison:

SEIDLITZ MIXTURE.

No.	Weights in Grammes.	Results of Qualitative Tests.	Per Cent. Sodium Bicarbonate.	Per Cent. Rochelle Salt.
1	10·676	Trace of sulphates.	24·962	74·731
2	10·323	Traces of iron.	30·731	68·818
3	10·948	Traces of sulphates and chlorides.	29·622	66·792
4	10·043	Traces of calcium and sulphates.	23·963	75·838
5	10·384	Traces of chlorides.	25·073	71·702
6	10·279	Traces of calcium and chlorides.	25·296	74·196
U.S.P.	10·333		25·000	75·000

TARTARIC ACID.

No.	Weight in Grammes.	Qualitative Tests.	Estimation.	
1	2·102	Traces of lead and sulphates.	99·66	
2	2·308	Sulphates and traces of calcium.	100·07	
3	2·679	Sulphates.	99·18	
4	2·673	Sulphates, traces of lead and calcium.	100·05	
5	2·253	Traces of lead and sulphates.	99·98	
6	2·308	Sulphate and trace of lead.	100·04	
U.S.P.	2·250			

Comments.—The tartaric acid, as is seen by the table, is almost uniformly of good quality.

The weights of the Seidlitz mixture show quite a little carelessness in weighing or measuring, and the results of analysis show that there is also considerable carelessness in making up Seidlitz mixture. Numbers 3 and 4 especially show this. It will be noticed, by adding up the percentages in numbers 3 and 5, that they are quite a little low. These samples both showed tests for chlorides, which were, however, found to amount to but a small fraction of a per cent. It was noticed that these samples were particularly caked, indicating that the low percentage might possibly be due to adhering moisture.

They, together with a portion of C.P. Seidlitz mixture, were then dried at 100° with the following results:

C.P. sample, loss = 18·805 per cent.
No. 3. " " = 20·048 "
No. 5. " " = 21·735 "

It is observed that the loss in number 3 is 1·243 per cent. more than the C.P., and in number 5 is 2·93 per cent. more. This does not quite account for the entire shortage, but it is enough to show that it is in all probability the cause.

To verify this conclusion a portion of C.P. Seidlitz mixture was triturated in a mortar with a quantity of water equivalent to the shortage in per cent., and to all appearances it remained a dry powder, caking when wrapped up and laid away.

Upon examination of the work and results just set forth it will be seen that for all practical purposes the Rochelle salt might be obtained by difference between the entire weight taken and the

sodium bicarbonate found. Therefore, for all commercial purposes, a Seidlitz-powder analysis consists in making a CO_2 determination, calculating the sodium bicarbonate therefrom, and (providing the qualitative test shows no contaminating impurities) determining the Rochelle salt by difference.

Before concluding, it might be well to state that designs for carbon-dioxide apparatus are to be found in nearly all reliable text-books, and many of them can be simply and quickly constructed.

SOLUBILITY OF COMPRESSED TABLETS.

By Anthony M. Hance.

Among the useful forms of medicine adopted in recent years there is none of greater importance and value than compressed tablets. Like all innovations in medicine, their adoption was somewhat slow. The physicians' requirements could very readily be supplied by pills, either gelatin- or sugar-coated, of which a large variety of combinations then existed.

The tablet form of medicine possesses important advantages not to be secured otherwise, such as minimum of bulk, certain and more rapid solubility and quicker therapeutic action. Certain combinations which readily undergo chemical change in the presence of moisture can be made into tablets to better advantage than into pills. Certain conditions may be successfully treated with medicine in tablet form, when pills would be impracticable, as, for example, where a continuous local effect is desired.

The purpose of this paper is to call special attention to the one all-important and absolutely indispensable quality of all scientifically compressed tablets, namely, solubility. Upon this one quality alone the tablet, as a form of medicine, stands or falls.

A tablet may be made ever so accurately and conscientiously with respect to purity of materials, skill in manipulation, a faultless check-system to guard against errors, uniformity in weight and size and handsome appearance; but, if the one quality of solubility is wanting, it is not a good tablet.

In the early days of tablet manufacture, the importance of solubility was under-estimated. The distinct advance was thought to be in the compression of the drug, thus presenting the medicament independent of the usual substances required to make a pill mass. The essential quality was permanence of form.

It seemed sufficient to compress the drug with such firmness that the finished product would not crumble from age nor break from attrition in handling or transportation. This was a mistaken idea. Such tablets were improperly made, and no more certain to produce the desired therapeutic effects than improperly made mass pills.

The distinct advance of compressed tablets over other forms of medicine lies in the fact that they present the drug in permanent and accurate subdivision and soluble form, and the up-to-date tablet is nothing if it does not possess the quality of ready solubility.

Firmness, or that degree of hardness which gives form and permanency to tablets, is essential in all well-made tablets, but neither prevents nor assures solubility.

A tablet which may be readily crushed with the fingers may or may not possess the proper degree of solubility, while it is generally not firm enough to be especially serviceable.

The term solubility as applied to tablets indicates power to disintegrate rather than power to form solutions. It refers to the tablet mass solely, the medicament of which is frequently one or more insoluble drugs, as, for example, calomel, charcoal, etc.

A tablet is soluble when, in the presence of the proper medium, it promptly disintegrates, thus liberating in a minutely subdivided condition the medicament it bears.

The degree of solubility is easily influenced by the nature of the component part. Thus solid extracts, resinous substances and certain drugs, such as reduced iron or corrosive sublimate, make tablets which disintegrate more slowly than others containing dissimilar substances. Tablets of corrosive sublimate are rendered more freely soluble than they would otherwise be by the addition of substances which favor solution, as, for example, muriate of ammonia.

In certain tablets solubility is relative, and quite unavoidably so. In others it is intentionally of slow degree. Throat tablets, in which by slow disintegration a continued local effect is sought, are familiar examples of the latter. In tablets for making extemporaneous solutions, and in hypodermic tablets especially, rapid disintegration and solution are desirable.

The determination of this solubility is a matter of considerable importance. The process is, apparently, quite simple. Drop a properly made tablet into a quantity of water and note the result. Immediately the form of the tablet changes and disintegration rapidly follows.

When this action occurs in the stomach the medicament is in the best possible form for speedy solution and absorption.

The tablets arranged before you for your careful and intelligent inspection, you will observe, possess this quality of free solubility or disintegration, and yet are remarkably firm or hard.

To obtain the results here displayed, it has been necessary to study the characteristics of each tablet batch separately, as well as its intended use and form—as, for instance, an ordinary tablet for the same purpose as a pill, a tablet triturate, a hypodermic tablet—and by repeated experiments determine the special method of manufacture which yields the best results. There is no one rule which can be applied to all tablets with uniformly good results. As each combination has distinct individuality arising from the nature of its component parts, so each kind of tablet requires its own special treatment to yield the most desirable degree of solubility.

A general treatment applies only in the manufacture of such simple and compound tablets as chlorate of potash, soda-mint, muriate of ammonium, and the class designated "throat tablets," in which quick solubility is neither sought nor desired.

PROGRESS IN PHARMACY.

A REVIEW OF SOME ADVANCES MADE DURING THE PAST YEAR.

By M. I. Wilbert.

After reading an interesting book, it is sometimes well to allow the subject-matter to pass in review before our mind's eye so as to impress the more interesting and important points on our memory in a connected and methodical way.

The happenings of a day, a week, or a year are like the records of a book, and if at the close of any specified period we allow the memory of these happenings to pass again through our mind, we will not only be the gainer, by having them impressed more vividly and indelibly on our memories, but we may, in addition, assort the various facts into groups or classes, so as to facilitate our retaining them for future use and reference.

The opening year of the twentieth century has passed into history, and has left us, as a heritage, a wealth of theories and facts that have been discovered and gathered together by the assiduous toil of many earnest workers in the various fields of scientific research.

It is our purpose, in this short paper, to bring before you some of the happenings of this past year that are especially interesting to us as pharmacists. It would, of course, be futile for us to attempt to review even a single branch of research thoroughly, so we will content ourselves by looking about and picking out for review just a few of the more prominent and interesting facts in two subjects or classes that we as pharmacists are, or should be, particularly interested in. These are, in the first place, the bibliography of pharmacy, especially the pharmacopœias and their accompanying books or commentaries, and then just a passing glance at some of the new drugs, or new uses for old drugs. In attempting so wide a field we will be compelled to ignore almost entirely the great amount of valuable information that has appeared during the year in the pharmaceutical journals, and can only mention briefly the lines that have been more thoroughly cultivated by the various contributors.

Numerous papers have appeared on the subject of standardizing drugs and preparations, and many ingenious methods have been brought forward to simplify the necessary processes, and to increase the accuracy of the ultimate results. In this connection we should like to call particular attention to a paper by Linde (*Apothkr. Zeitg.*, 1901), in which, under the able direction of Professor Beckurts, the author gives a summary of the methods of extraction, and the menstrua or solvents proposed by various authorities for assay processes. The review includes processes for sixteen specific drugs, and numerous reviews of general methods. Seventy-eight separate papers by sixty-five different authors are included in this review.

The use of the microscope has been the theme of many interesting papers. The value of this instrument in recognizing drugs or their adulterations is now generally recognized, especially in Germany, where the national pharmacopœia includes many more or less accurate descriptions of drugs in the powdered state. It is from Germany too that we would naturally expect the greatest advances along this line. During the year two very important books on this subject have come from the German press: "Die Mikroskopische Analyse der Drogenpulver," by Prof. Dr. L. Koch, and a second edition of "Schimpers Anleitung zur Untersuchung der Vegetabilischen Nahrungs und Genussmittel."

Adulterations have of course been the constant care of a host of watchdogs in the pharmaceutical profession, and the reports from

these able and disinterested workers have called attention to many crude as well as refined methods of contaminating drugs and foodstuffs with inert and sometimes dangerous materials. One of the most abominable and despicable methods of adulterating or cheapening galenical preparations is by the substitution of methyl alcohol in some of the preparations generally sold for domestic consumption. We will have more to say on this subject later under the title of Methyl Alcohol.

Pharmacopœias, representing as they do the sum total of progress or research available to the respective revision committees, or commissions, are always objects of considerable interest to the scientific pharmacist; and especially is this true of us at the present time, for we are all more or less interested in the revision and improvement of our own United States Pharmacopœia, and the scientific or practical success or failure of other pharmacopœias may indicate subject-matter to adopt or avoid in our own.

Among the pharmacopœias more directly interesting to us is that of the other half of the English-speaking world, the British Pharmacopœia. The field of usefulness for this work has been extended by the republication and elaboration of the Indian and Colonial Addendum. This may be considered as the forerunner of the proposed British Empire Pharmacopœia. This addendum includes 122 titles: fifty-three of vegetable origin; two animal (Hirudo Australis and Mylabris); one chemical (Pyrogallol), and sixty-five galenical preparations. Articles designed for a particular colony, and differing from the same class or kind of article official in the body of the pharmacopœia, are only to be used in the colony or zone for which they have been designed, and are not to be used or dispensed in any other portion of the empire unless especially ordered.

To avoid misunderstandings, the empire has been divided into seven districts or zones: (1) India, (2) African Colonies, (3) Australian Colonies, (4) Eastern Colonies, (5) Mediterranean Colonies, (6) North American Colonies, (7) West Indian Colonies.

"The Pharmacopedia," by Edmund White and John Humphreys, is a commentary on the British Pharmacopœia. This book has been ably reviewed in the January (1902) number of the AMERICAN JOURNAL OF PHARMACY, and deserves more than a passing notice. Pharmacopœias of all lands are apt to be rather above the capacity and abilities of the average pharmacist, and it is for commentaries

of just this kind that there is a need and a want—a book that will aid and explain the obscure and knotty problems of the standard of authority. Works of this kind tend to bring the pharmacist up to the level of the Pharmacopœia, instead of doing as some supposed commentaries do, bring the Pharmacopœia down to the level of the average and even mediocre dealer in drugs and patent medicines.

The Germans have for years had commentaries along the lines followed by the Pharmacopedia. We need but refer to the well-known work by Hirsch, in which he was assisted in the later edition by Dr. Alfred Schneider. The fourth edition of this popular book is now in press, being published under the able direction of Drs. A. Schneider and P. Süss as a commentary to the fourth edition of the "German Pharmacopœia." Another German commentary that is being issued at the present time is that of Jehn and Crato. Both of these works, however, are rather comprehensive. For such of the members of the German pharmaceutical profession as do not feel able to subscribe to these more or less pretentious and expensive works, and still wish to have something more available for reference than the very able and thorough aids and criticisms published in the German pharmaceutical journals, they have the choice of "Chemische Reagentien und Reactionen des Deutschen Arzneibuches IV," by Holdermann and Kendle, or the popular "Anlitung zur Erkennung und Prüfung aller im Arzneibuch für das Deutsche Reich (4te Aufgabe) Aufgenommenen Arzneimittel," by Dr. Max Biechle.

The fourth edition of the German Pharmacopœia has been most thoroughly discussed and criticized, not only in the commentaries and the current pharmaceutical literature, but also in the publications of the large drug houses and manufacturers in their so-called "Handels berichte" many of the discrepancies of the pharmacopœia have been commented on, and much valuable information been contributed in this way.

The requirements of the German Pharmacopœia are of such a nature that many German apothecaries have found it advisable to attend short post-graduate courses in practical work with the microscope and chemical burette. These courses, it appears, are held in large university towns, and cover about twelve working days. The work with the microscope is largely devoted to the consideration of

the use of the "micrometer ocular" for measuring starch and aleurone grains. The series of chemical tests usually include assay processes for ipecac, cinchona, hydrastis and nux vomica, and also the determination of the saponification and iodine numbers of fixed or fatty oils.

The *Deutschen Apotheker-Verein* published during the year its "Homeopathic Pharmacopœia." This book was published by the society with a view of securing greater uniformity in homeopathic preparations. It has not been officially recognized by the Imperial Government nor any of the smaller states outside of Prussia and Wurtemberg. Dr. William Schwabe has also published a new edition of his "Homeopathic Pharmacopœia." As might be expected, there is considerable difference of opinion between the followers of Schwabe and the Society of Apothecaries as to which book is the more reliable and trustworthy interpreter of homeopathic principles.

The eighth edition of the "Swedish Pharmacopœia" (Svenska Farmakopen) has recently come from the press. This is the first revision of this book since 1879, and, as may be expected, the book presents many marked changes. Following the example set by other leading works of this kind, the text of the book is in the vernacular, while the titles of the various articles are in Latin. The work appears to be thoroughly up to date, and includes among other innovations qualitative and quantitative chemical tests for digitalis, cinchona, opium, belladonna, hyoscyamus, lobelia, ipecac, and nux vomica. The essential or volatile oils have had considerable attention, and a variety of tests are given for possible adulterations. For the fatty oils the saponification and iodine numbers are given. The drugs of animal origin are restricted to wax, lard, spermaceti, and suet. An innovation for this pharmacopœia is the introduction of fluid extracts.

At the end of the work appear various appendices, including lists of the reagents mentioned in the text, maximum doses of potent remedies, atomic weights (O = 16) and two indexes. One of these tables deserves particular attention: it is a maximum dose-list of active drugs for domestic animals; it includes thirty-five titles of drugs and preparations and the maximum doses for horses, cattle, sheep, swine and dogs.

The "Swiss Pharmacopœia" is undergoing a revision, and the revision committee, consisting of eleven members, five apothecaries,

one pharmacologist, four physicians and the President of the Federal Sanitary Bureau at Bern, has published for consideration and debate two lists of drugs and preparations that are proposed as additions or changes in the forthcoming work. The two lists comprise a total of eighty-three titles; among others, a general title or proposition for serums. This particular proposition is rather interesting. The committee proposes the adoption of serums under the following headings:

(1) Tuberculin, Koch.
(2) Serums, general and special.
(3) Antidiphtheritic serum.
(4) Antitetanic serum.
(5) Antistreptococcic serum.
(6) Vaccine virus.

In this connection it is proposed to have an official system of tests and standardizing under control of the Swiss Gesundheitsamt. Of the remaining eighty-three titles, twenty-nine are of proposed new additions, among them twenty-one chemicals, four plant drugs, and four galenical preparations. Among the chemical titles are bromoform, ethyl chloride, ethyl morphine hydrochlorate and sodium theobromine salicylate.

Another interesting work in this connection is the "Universal Pharmacopœia," by Dr. Bruno Hirsh. This interesting book consists of a conglomerate of twenty-eight different authoritative works or pharmacopœias. The first volume of the second edition of this work has been issued, and the second volume is said to be ready for press. This is probably one of the most interesting and valuable books in pharmaceutical literature, and it is to be regretted that it is not more readily available for reference and comparative study.

New remedies of a patented or proprietary nature are increasing at a rate that makes it practically impossible to keep in touch with the nomenclature, to say nothing of becoming familiar with the composition or uses of the articles themselves. One apparently good feature of this over-supply is the gradual awakening of members of the medical profession to the fact that many of these supposed wonderful discoveries are nothing more than commercial ventures. No less an authority than Professor Kobert, of Rostock (*Aertz. Vereins blatt f. Deutschl.*), calls attention to the ever-increasing number and varied claims of these compounds, and inquires as to

where the practitioner should look for authoritative information. He admits that the medical journals are too apt to be swayed by their advertising pages, and that at best, reports and opinions of individual workers are of little value; and further, that few if any medical men have the courage to report their failures with new remedies. This latter fact has indeed been most unfortunate, as it has been the cause of untold disappointment and loss, not alone to the suffering patients, but also to the doctor, who, having been induced to try a certain highly recommended compound, fails absolutely to get the desired results, and concludes that either the man who was guilty of writing the glowing account of successful use was mistaken, or that he was pecuniarily interested. And while it takes a number of such experiences to make or have the proper effect, it is just a matter of time when the medical profession will awake to the necessity of having more than the say so of one or even half a dozen professional advertisers before they give aid to and prescribe a drug they know little or nothing about. In this respect the medical literature of the past year shows commendable progress over that immediately preceding. There are a number of reports of unsuccessful use of drugs, or the appearance of unlooked-for and disagreeable secondary actions of the drugs or chemicals employed.

Adrenalin.—The active principle of the suprarenal gland has played an important part in the medical and pharmaceutical literature of the year. Its chemistry and uses are well described by its discoverer in a recent number of the AMERICAN JOURNAL OF PHARMACY.

Agurin.—A double acetate of soda and theobromine is being brought forward as a substitute for and an improvement on diuretin. It is said to be free from the rather serious objection to the latter compound of causing more or less severe gastro-intestinal irritation.

Bromocoll.—A combination of bromine, water and gelatine, said to be dibromine-tannin-gelatin, is claimed to have all the sedative properties of potassium bromide without any of its disagreeable secondary effects. Mayr (*Deutsch. Med. Wochschrf.*, 1901) reports using this drug in cases of epilepsy, with favorable results. Dose, 2 to 8 grammes daily.

Cacodylic Acid.—The salts of this compound of arsenic are not increasing in popularity. Several fatal cases of poisoning have been

reported, and even French physicians admit that they do not always obtain favorable results. The alleged freedom from ill effects is due (*Apothkr. Zeitg.*, 1901) to the fact that the drug is largely eliminated with the fecal matter, without having been decomposed or changed in any way.

Chloretone is another of the new drugs that has not come up to the expectations of the average physician; not being soluble in water, it has not always met with success as a local anæsthetic. *Hedonal* has been reported on from various quarters; several authors object to the peculiar and disagreeable taste of the drug. Secondary effects are said to be not uncommon, but not serious; one of the more disagreeable is due to the fact that the substance is also a diuretic. This action is at times so pronounced that it interferes with continued sleep.

Hetol.—Sodium cinnamate. Kuhn (*Münch. Med. Wochschrf.*, 1901) considers that the improvement in cases of tuberculosis treated with intravenous injections of this drug was so slight that they may easily be accounted for by improvement in hygiene and surroundings. Gidion (*Deutsch. Arch. f. Klin. Med.*, 1901) comes to the same conclusion, and even reports several cases that have lost weight under treatment.

Honthin.—Frieser (*Therapist*, 1901) describes this compound as a combination of tannin with albumin and keratin. He has used it in thirty-two cases with favorable results and believes it to be half as powerful again as tannalbin. It is given in doses of from 0·5 to 1·0 three or four times a day.

Ichthyoform is a combination of ichthyol with formaldehyde. Average dose 1·0 to 2·0, used in diarrhœa due to intestinal tuberculosis, also used with good effect in the diarrhœa of typhoid fever. It is said to combine the analgesic and astringent action of ichthyol and the exceedingly energetic influence of formic aldehyde.

Igazol, supposedly a mixture containing formaldehyde and iodoform, has been reported on unfavorably by Wolff (*Deut. Med. Wochschrf.*, 1901).

Purgatin, the diacetate of anthrapurpurin, is one of the most interesting possibilities in the field of synthetic chemistry. It is probably the first compound that promises to be a more or less efficient aperient or cathartic. It was at first marketed under the name purgatol, and is an orange-yellow crystalline powder, insol-

uble in water or dilute acids, but decomposed by dilute alkaline solutions (producing a solution of dark violet-red color). It probably passes the stomach unchanged, decomposing only in the intestinal canal. In doses of 0·5 it is said to produce a mild evacuation of the bowel in from twelve to eighteen hours without griping. It is said to have the same debilitating effect on the intestines that has been noted with other cathartics, especially rhubarb. One peculiar feature connected with this new drug is the fact that it imparts to the urine a blood-red color. The patient should be made acquainted with this fact so as to avoid unnecessary alarm. Stadelman (*Deutsch. Aerzte Zeitg.*, 1901) says that the dose advised by the manufacturers is too low, and that 2·00 is nearer a normal dose.

Silver.—Organic salts of this metal threaten to increase indefinitely, despite the fact that they have been repeatedly proven to be more or less inert and ineffective. So far, no satisfactory and reliable substitute for nitrate of silver has been offered.

Uresin.—The double citrate of lithium and urotropin is being suggested as a diuretic and urinary antiseptic. It should not be mistaken for the older, though not popular urosin, a combination of lithium and quinic acid.

Urol.—A chinate or quinate of urea is being brought forward as a remedy for uric acid diathesis. Dose from 2·0 to 4·0 grammes.

Urotropin, cystogen and *formin*, under which names various firms are marketing hexamethylene tetramine, have been the subject of considerable comment and discussion. It would appear from the published reports that this compound is not as harmless or as reliable as the earlier reports would indicate. Brown (*Brit. Med. Jour.*, 1901) reports two cases of hematuria after use of urotropin in doses of 0·6 three times a day. Many other reports of a similar nature have since appeared, and it will be well to exercise considerable caution so as to prevent any possible abuse of this remedy by self-medication.

Apomorphine.—Douglas (*Wiener Med. Presse*) recommends this drug as an efficient and safe hypnotic. Hypodermatic injections of 0·002 are said to produce sleep within five minutes. It is said to have the advantage of not producing a drug habit, as in larger or repeated doses it produces nausea and vomiting.

Caffeine.—Ferraby (*La Semaine Medicale*, 1901) recommends this

drug in cases of poisoning by carbolic acid. He has given 0·15 hypodermatically with immediate favorable results.

Calcium iodate has been recommended as a substitute for iodoform. Mackie (*Merck's Archives*) considers it to be an excellent antiseptic, preventing hypergranulation and the formation of pus. It can also be used in solution for washing out the bladder, vagina and uterus. It may also be used in gargles and mouth-washes, or may be given internally to check fermentative processes in the stomach. Dose, 0·2 to 0·3.

Carbolic Acid.—The use of alcohol instead of water to liquefy this chemical, gives a solution that mixes readily with fixed oils without separating or producing a turbid mixture. It is also more permanent, not crystallizing in cold weather.

Formaldehyde.—The increased use of this compound has increased the possible danger of poisoning from accidental or other causes. *Therapeutische Monatshefte*, 1901, recommends the use of liquid ammonia well diluted, aromatic spirits of ammonia, or even liquid ammon. acetate, the theory being the reduction of the formaldehyde to hexamethylene tetramine, a comparatively harmless substance.

Horse-Chestnuts.—Schurmeyer (*Therap. Monatsh.*, 1901) recommends a fluid extract of horse-chestnuts as an external application in cases of rheumatism, neuralgia and painful affections of the skin; also as a gargle in 1 and 2 per cent. solutions. The author also claims that the saponin contained in the horse-chestnut is not poisonous.

Hydrocyanic acid gas has been recommended as a disinfecting agent and germicide. It has been in use as an insecticide, especially in greenhouses; also in sleeping cars, to rid them of vermin.

Ipecac root has been the subject of much investigation and discussion. It appears that the total alkaloids of Brazil and Carthagena ipecac are about the same, but their composition varies considerably, the Brazilian root being richer in emetin, while cephaelin predominates in the Carthagena variety. Both these compounds are emetics, with the consensus of opinion in favor of cephaelin as being the more active. In this connection it may be interesting to note that the Carthagena root is excluded from the German Pharmacopœia by the limitation of the size of the starch granules, the starch granules of the Carthagena root being much larger than those of the official Brazilian.

Methyl Alcohol.—Suggestions that have been made from time to time as to the possible use of this compound in pharmacy have, unfortunately, been adopted by a class of dealers that are always anxious to increase their profits regardless of any hazard or risk that may be incurred by their customers. Not alone in tincture of iodine, soap liniment, and other preparations used for external purposes, it has also been found in tincture of ginger, essence of peppermint, and other drugs and flavoring essences usually sold for popular consumption. Würdeman (*Amer. Med.*, 1901) reports several cases of blindness resulting from the use of this compound, and also gives a summary of a number of other cases that have been recently reported. Sieker (*Chem. Zeitg.*, 1901) suggests as a reliable test the reduction of cupric oxide by vapor of methyl alcohol and the production of formaldehyde, readily recognized by its peculiarly pungent and penetrating odor.

Oleic Acid.—Artault (*Rev. Therap. Med. Chirurg.*, 1901) suggests the use of purified oleic acid in cases of hepatic colic due to gallstones. He gives the acid in doses of 0·5 to 1·0, and in cases where the attacks occur at intervals of a month or more he suggests giving the remedy for from ten to fourteen days.

Picric acid is being brought forward as an external dressing and a remedy in affections of the skin. It has proved itself to be especially valuable in superficial burns, acute eczema, and herpes zoster; used in ½ or 1 per cent. solution.

Phosphorated oil, as a substitute for this preparation, when it is to be used for internal purposes, Escalle (*Zeitschr. des Allgemein. Oestr. Apoth. Verein*, 1901) proposes glycerin as the solvent. He produces a 1 per cent. glycerin-alcohol solution by allowing 10· phosphorus to be heated under 100· glycerin until melted, then shake until cool, add 400· glycerin and 500· alcohol 96 per cent.; keep in a cool, dark place.

Quinine.—Binz (*Therap. der Gegenwart*, 1901) recommends large doses of a quinine salt with cold baths in cases of typhoid fever. He thinks that quinine is an active poison to the lower organisms, and gives the drug in doses of 1·0 every other evening.

Salicylates.—Wolff (*Chem. Zeitg.*, 1901) reports that freshly precipitated hydroxids of iron, aluminum and copper are soluble in solutions of sodium or ammonium salicylate. It is said that the copper sodium salicylate reacts similar to Fehling's solution with

substances containing sugar. And it is further suggested that the iron sodium salicylate might be of some use in medicine.

Senna.—Alexandria senna has been demonstrated to contain upward of 20 per cent. more of the supposed active principle, oxymethyl anthra chinon, than the corresponding leaves of the Tinnevelly variety. The former should, therefore, be considered the more efficient.

Strophanthus.—According to F. Feist (*Ber. d. Deut. Chem. Gesells.*) there is a marked difference in the preparations of this drug when made from Strophanthus Kombe, or Strophanthus hispidus, as they vary considerably in the kind and amount of the glucoside contained in them, the pseudostrophanthin of Strophanthus hispidus being twice as active as Strophanthin contained in Strophanthus Kombe.

Wines.—Dr. Carl Rundquist (*Apoth. Zeitg.*, 1901) has made a series of experiments with the idea of replacing the official wines of the "German Pharmacopœia" by sweet wines in the making of official preparations of medicated wines. According to his experiments Port wines and wines of this character having a high percentage of sugar appear to have greater solvent properties for alkaloids and active principles of drugs than sherry and Malaga wines.

RECENT LITERATURE RELATING TO PHARMACY.

NEW REMEDIES OF 1901.[1]

Abroma Augustum—See Olut Kombool.

Acetamidophenoxylacetamide—Antipyretic.

Acetamidophenoxylacetamide-chloral—Sedative.

Acetanilidsulphonsodium—Soluble antipyretic.

Acetospirin—Acopyrine. Compound of aspirin and antipyrine. Antirheumatic. Dose: 0·5 grammes, 5–6 times daily.

Acetylated Methylenediguaiacol—See Euguform.

Acid, Cinamylcacodylic—See Cinamylcacodylic acid.

Acid, Iodosobenzoic—Local Antiseptic.

Acid, Morphoxylacetic—See Morphoxylacetic acid.

Acid, Orthohydrazineparabenzoic—See Orthine.

Acid, Salolorthophosphinic—See Solvosal.

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[1] *Merck's Report*, January, 1902.

Acopyrine—See Acetospirin.

Acrolein-Sulphurous Acid—Local antiseptic, as wash, ointment, or dusting powder.

Adrenalin—1·1900 solution. Active principle of suprarenal capsule.

Aethiopian Pepper—See *Xylopia aethiopica.*

Agurine—Theobromine-sodium and sodium acetate. Diuretic. Dose: 0·25–0·5 gramme.

Albargin—Silver gelatose. Antiseptic and antigonorrhœic in 0·1–0·2 per cent. solution.

Albizzia Anthelmintica—"Musena" bark. African plant used as an anthelmintic.

Alboferrin—Iron-phosphorus-albumin compound. Tonic and nutrient.

Algicide—Anodyne and antiphlogistic.

Alkaseptol—Antiseptic, germicide, and detergent.

Alpha-Eunol—Compound of alpha-naphtol and eucalyptol. Antiseptic.

Alummatine—Antiseptic surgical dressing.

Amyl Salicylate: $C_6H_4OH.CO_2C_6H_{11}$. Antirheumatic and sedative.

Anaemin—Solution of "iron-pepsin saccharate." Antichlorotic.

Anthrapurpurin Diacetylester—See purgatol.

Anticholerin—Cholera antitoxin solution. Disinfectant.

Antiformin—Disinfectant.

Antipyrine Salicylacetate—See Tyrosal.

Aponia—Dental anæsthetic.

Aquinol—Disinfectant.

Avenose—Infant food.

Azymal—Buccal disinfectant.

Bacillol—General disinfectant.

Beta-Eucaine Acetate—Local analgesic and anæsthetic. Used in 2 per cent. solution.

Bioplasm—Antitubercular, antimalarial, and febrifuge.

Bismutal (Bismutol)—Mixture of sodium salicylate and soluble phosphate. Antiseptic.

Bismuth Cinnamate—See Hetoform.

Bismuth Dilactomonotannate—See Lactannin.

Bismuth Lactogallate—Used like bismuth preparations.

Bismuth Lactotannate—See Lactannin.

Bismutol—See Bismutal.

Bismutose—Bismuth-albumin preparation. Gastro-intestinal and local antiseptic. Dose: ½–1 drachm for children.

Bocyl—Alcoholic solution of cinnamic and boric acids. Buccal disinfectant.

Boliformin—Compound of formaldehyde and aluminum silicate. Dusting powder for wounds, and veterinary siccative.

Boric Acid Ethyl-Ester—See Borogen.

Borobenphenene—Antiseptic and germicide.

Borogen—Boric-acid ethylester. Disinfectant for respiratory organs. Used by inhalation.

Branalcane—Disinfectant for diphtheritic and infective diseases.

Bromyl—Nervous sedative and antiepileptic.

Cacodiacol—Guaiacol cacodylate.

Calcinol—Calcium iodate. Succedaneum for iodoform.

Calcium Glycerinoarsenate—Arsenical medicament. Dose: 0·01 grammes.

Calcium Iodate—See Calcinol.

Calystegia Soldanella—Cathartic. Dose: 3–4 grammes of powder; of resin, 1·5 grammes.

Camphoric-Acid Phenetidid—Compound of camphoric acid and paraphenetidin. Antipyretic and antihydrotic.

Canutillo—See *Ephedra nevadensis.*

Caynote—See *Ephedra nevadensis.*

Cerevisine—Desiccated yeast, used like beer yeast in boils, furuncles, etc.

Chloromethylmenthyl Ether—Forman. Compound of formaldehyde, hydrochloric acid, and menthol. Used in coryza.

Chloropepsoid—Remedy for gastritis, gastric neuroses, and alimentary disturbances.

Choclon—A "vegetable milk" used in Argentine Republic as a nutrient.

Chrysolein—Sodium fluoride.

Chuchuarine—Alkaloid from *Senecarpus anacardia.* Aphrodisiac.

Cinchonine Dihydrochlorate—Antipyretic, antiseptic, and malarial prophylactic.

Cinchonine Sulphocresotate—Antipyretic, antiseptic, and malarial prophylactic.

Cinnamyl-cacodylic Acid—Used like cacodylates.

Colyticine—Parasiticide, antiseptic, and disinfectant.

Contrayerva—See *Dorstenia brasiliensis.*

Corpulin—Antiobesity tablets, said to consist of extract bladderwrack, tamarinds, and cascara sagrada.

Cretamethyl—Local antiphlogistic.

Cuprargol—Copper-albumin compound: Antiphlogistic and secretory stimulant. Used in 1–5 per cent. solutions.

Cypridol—1 per cent. solution of "nascent" mercuric iodide in neutral aseptic oil. Dose: 0·2 gramme.

Didymium Salicylate—See Dymal.

Dioxogen—Trade name for hydrogen dioxide.

Dithan—Trional.

Dorstenia Brasiliensis—Contrayerva. Digestive tonic and diaphoretic. Dose: Tonic, 2 grammes; diaphoretic, 4–8 grammes daily.

Doundaké—*Sarcocephalus esculentus.* Bark is tonic, febrifuge, and astringent. Dose: Wine (3 per cent.), 1–2 fluid ounces; extract, 2½–3 grains; bark, 50–60 grains; aq. extract, 3–4 grains.

Doundakine—Alkaloid from Doundaké (q. v.). Quinine substitute. Dose: 3–4 grains.

Dymal—Didymium salicylate. Antiseptic and siccative.

Dymol—Remedy for intestinal disorders. Dose: 1–3 grains.

Enterol Carbonate—Carbonic-acid ester of enterol (mixture of cresols used as an intestinal antiseptic).

Entona—White-wheat-gluten suppositories.

Ephedra Nevadensis—Caynote; Canutillo; Tapopote. Blood purifier and antigonorrhœic. Dose: Teaspoonful of fluid extract.

Erysimin—Glucoside from seeds of *Erysimum.* Physiological properties like those of digitalin.

Esanofele—Antimalarial.

Euguform—Acetylated methylenediguaiacol. Antiseptic vulnerary.

Enophtalmin—Improper spelling (in many journals) for euphtalmin.

Eupyrin—Paraphenetidin vanillin-ethylcarbonate. Antipyretic. Dose: 1–1·5 grammes.

Farola—Nutrient.

Floricin—Ointment base.

Formaldehyde-soap—Compound of formaldehyde and soap. Disinfectant.

Forman—See Chloromethylmenthyl ether.

Gasterin—Preparation made from stomach of the dog, and used like pepsin.

Germiletum—Compound antiseptic solution.

Giaourdi—Preparation of fermented milk. Nutrient.

Glycine Subterranea—See Voandzou.

Glycobenphene—Remedy for cutaneous diseases.

Glycogenol—Substance obtained from animal organism, and nearly allied to glycogen. Used in tuberculosis and typhoid fever. Dose: 0·2 gramme hypodermically or per os.

Glycosolvol—Peptonized theobromine-trypsin oxypropionate.

Guaiacol Cacodylate—See Cacodiacol.

Heliosin—Indefinite mixture of various inorganic salts with keratin. Antisyphilitic.

Hemoglobin Albuminate—See Perdynamin.

Hermophenyl—Mercury phénoldisulphonate. Bactericide and antiseptic in 1–5 : 1000 solution.

Hetoform—Bismuth cinnamate, $Bi(C_9H_7O_2)_3B_2O_3$.

Hydrargotin—Mercury tannate.

Ichthosin—Ichthyol compound of eosine used in skin diseases.

Isopilocarpine—Isomer of pilocarpine. Action like that of pilocarpine, but much weaker.

Impatiens Fulva—See Jewel-weed.

Iodized Meat Powder—Succedaneum for iodides and organic iodine compounds for internal use.

Iodochloroxyquinoline—See Vioform.

Iodogenol—Compound of iodine and peptonized albumin. Succedaneum for iodine preparations for internal use.

Iodokol (or Iodocol)—Iodine-guaiacol compound. Used in pulmonary tuberculosis, tubercular pneumonia, croupous pneumonia, and bronchial asthma. Dose: 0·2–0·4 gramme 4–5 times daily.

Iodosobenzoic Acid—Local antiseptic.

Iron Paranucleinate—See Triferrin.

Ironal—Ferruginous preparation containing 80 per cent. iron.

Jamrosin—Fluid extract of an East-Indian Myrtaceæ used as an antidiabetic. Dose: six drops thrice daily.

Jequirtol—Sterile abrin solution of uniform physiological action. Used for inducing conjunctival inflammation.

Jewel-weed—*Impatiens fulva.* Freshly expressed juice is an antidote to poison-ivy.

Kaki— Japanese persimmons, recommended for stubborn vomiting in pregnancy, and in diarrhœa.

Kanagugi—*Lindera erythrocarpa.* The fluid extract is used by the Japanese in secondary syphilis. Dose: teaspoonful.

Karos—South African plant used in dysentery and in ulcerative and hæmorrhagic intestinal affections.

Kreospinal—Preparation of creosote and spinach. Remedy for phthisis.

Kretol—Surgical dressing, antiseptic, and germicide.

Lactanin—Bismuth dilactomonotannate. Used in diarrhœa and malaria. Dose: 1–5 grammes daily for children.

Levico-Ocher—Iron-arsenic mud from Levico. Used as hot application in neuralgia, inflammatory processes and exudates, and also sexual diseases.

Lindera Erythrocarpa—See Kanagugi.

Liquor Thiophosphini—Solution containing chiefly potassium guaiacol sulphonate. Dose: 5–10 grammes.

Lithrea Caustica—Litre. An Anacardiaceæ found in Chili, and used in form of a tincture as a counter-irritant.

Litre—See *Lithrea caustica.*

Lozon—Trade name for hydrogen dioxide.

Lycresol—Soap solution containing crude cresol. Antiseptic.

Mangrove—*Rhizophora mangle.* Used in leprosy.

Melan—"Condensation product" of the buds, leaves, and twigs of *Melilotus cæruleus.* Cicatrizant and vulnerary.

Melonemetin—Bitter principle from melon. Emetic and purgative.

Menthyl Acetoacetate—$CH_3C(OH):CH.COOC_{10}H_{19}$. Bactericide.

Mercuramin—Mercury ethylenediamine citrate.

Mercury Cacodylate—Antitubercular. Dose: 0·03 gramme per day intramuscularly.

Mercury Ethylenediamine Citrate—See Mercuramin.

Mercury Phenoldisulphonate—See Hermophenyl.

Methylene Creosote—See Pneumin.

Methylene Diguaiacol—See Pulmoform.

Methylene Diguaiacol, Acetylated—See Euguform.

Modoformol—Antiseptic dressing.

Morphine Caseinate—Soluble compound of morphine and casein.

Morphoxylacetic Acid—$C_{17}H_{18}NO_3.C.H_2.COOH$. Narcotic, like morphine, but weaker.

Muscarium—Extract of *Amanita muscaria*. Used in digestive atony. Dose: 0·01–0·05 gramme.

Musena—Bark of *Albizzia anthelmintica*. Anthelmintic.

Mycoserum—Muscle juice. Nutrient antitubercular.

Oenotannol—Tuberculosis remedy consisting of tannic acid and grape juice or grape pulp.

Oleïte—Jelly-like ointment base obtained by action of sulphuric acid on castor oil.

Olut Kombool—*Abroma augustum*. East-Indian remedy for dysmenorrhœa.

Oroxylin—Crystalline substance from *Oraxylon indicum*. Astringent and tonic.

Orthine—Orthohydrazineparabenzoic acid. Phenylhydrazine derivative. Antipyretic. Dose: 4–7 grains.

Orthohydrazineparabenzoic Acid—See Orthine.

Ovos—Succedaneum for meat extract, prepared from yeast.

Oxytoluylmethylvinyldiacetonealkaminehydrochlorate—See Enophtalmin.

Pancreon (Pankreon)—Pancreatin-tannin compound. Tryptolytic, used in gastro-intestinal digestive disturbances. Dose: 0·3–0·5 gramme, thrice daily.

Paraphenetidin-Vanillin-Ethylcarbonate—See Eupyrin.

Parietin—Chrysophanic acid.

Pegmin—Species of rennet for rendering cow's milk easily digestible.

Pelargonium Flabellifolium—South-African plant, the root of which is used as a remedy in dysentery.

Pentodyne—$4(Na).C_{34}N_5H_{40}.O_{10}.OH(?)$. Analgesic, antipyretic, and neuralgic. Dose: 2–10 grains.

Perdynamin—Hemoglobin albuminate.

Peroxine—Non-volatile (?) hydrogen dioxide.

Phenamide—Coal-tar derivative. Antipyretic and analgesic.

Phenol-Celluloid—Phenol-camphor solution of pyroxylin used as a varnish for protecting wounds, etc.

Phosphorylquinine—Quinine-phosphoric-acid ester.

Phrynine—Alkaloid extracted from cutaneous glands of several species of toad. Antiepileptic.

Pneumin—Methylene-creosote. Antitubercular.

Protan—Tannin-nucleoproteid. Antidiarrhœal. Dose: 20–30 grains.

Protose—Vegetable food for anemia, diabetes, obesity, dyspepsia, etc.

Pulmoform—Methylene diguaiacol. $CH_2(C_6H_3.OHOCH_3)$. Antitubercular.

Purgatol—Anthrapurpurin diacetylester. Mild purgative. Dose: 0·5–1 gramme.

Purgo—Phenolphtalein. Purgative. Dose: 0·1–0·6 gramme.

Pyramidon Camphorate—Succedaneum for antipyrine and pyramidon in tuberculosis. Dose: 1 gramme.

Quinine Acetylsalicylate—$C_{20}H_{24}N_2O_2.C_6H_4.O.C_2H_3O.COOH$. Quinine compound for internal use.

Quinine Phosphoric-Acid Ester—See Phosphorylquinine.

Quinine Salicylic-Acid Ester—See Saloquinine.

Quinine Methyldihydrazine Perchlorate—Compound obtained by fusing together quinine hydrochlorate, caffeine, and antipyrine.

Radal—20 per cent. solution of protargol.

Ramogen—Infant and invalid food.

Remarcol—Sodium fluoride.

Rheumatin—Salicylquinine (saloquinine) salicylate. Antirheumatic. Dose: 1 gramme.

Rhizophora Mangle—See Mangrove.

Saccharosolvol—Organotherapeutic preparation obtained by action of salicylic acid on diastatic ferment of pancreatic juice and spinal marrow of cattle.

Salicylquinine Salicylate—See Rheumatin.

Salicylic-Acid Benzyl Ester—External antiseptic.

Salinigrin—Glucoside from bark of *Salix nigra.*

Salolorthophosphinic Acid—Solvosal.

Saloquinine—Quinine ester of salicylic acid. Febrifuge and analgesic. Dose: 2 grammes.

Saloquinine Salicylate—See Rheumatin.

Sanatolyn—Disinfectant and deodorizer.

Sarcocephalus Esculentus—See Doundaké.

Sarton—Nutrient.

Selenopyrine—Product of reaction between potassium selenide and antipyrine "chloride."

Silver-Gelatose—See Albargin.

Sitogen—Vegetable-meat nutrient extract.

Sodium-Caffeine Salicylate—See Xanol.

Solvosal—Salolorthophosphinic acid.

Solvosal-Lithium—Compound of solvosal (q.v.) and lithium. Intestinal antiseptic and diuretic. Dose: 0·25–0·5 gramme: 3–5 grammes daily.

Solvosal-Potassium—Compound of solvosal (q.v.) and potassium. Intestinal antiseptic.

Tapopote—See *Ephedra nevadensis.*

Tartaric-Acid Diphenylester—Condensation product of tartaric acid and phenol. Antipodagric.

Tartrophen—Compound of phenetidin and tartaric acid. Used like citrophen.

Tetramethylcyanpyridon—Myotic.

Theobromine-Sodium and Sodium Acetate—See Agurine.

Theobromine-Trypsin-Oxypropionate, Peptonized—Glycosolvol.

Thiopyrine (Thioantipyrine)—Product of reaction between potassium sulphydrate and antipyrine "chloride."

Thymatol—Thymol carbonate. Tyratol. Anthelmintic. Dose: 2 grammes; 0·5–1 gramme for children.

Thymol Carbonate—See Thymatol.

Thymol Chlormethylsalicylate—Condensation product of thymol and chlormethylsalicylic acid. Antiseptic.

Triferrin—Iron Paranucleinate. Hematinic. Dose 5 grains three times daily.

Triphenylguanidine Guaiacolsulphonate—Local anæsthetic.

PHARMACEUTICAL MEETING.

The fourth of the series of pharmaceutical meetings of the Philadelphia College of Pharmacy for 1901–1902 was held on Tuesday, January 21st. Mr. William L. Cliffe, well known for his activity in pharmaceutical matters, presided.

The first speaker was Mr. Benjamin T. Fairchild, New York City, a member of the firm of Fairchild Brothers & Foster, who gave a very comprehensive paper on "The Evolution and Use of the

Digestive Ferments in Medicine" (see p. 53). The author treated of the genesis of the subject in its relationship to pharmacy and medicine and briefly referred to the brilliant researches of Spallanzani, Schwann, Kühne, Büchner, and others. Spallanzani was the first to make a distinction between peptic digestion and putrefaction; Schwann first demonstrated the existence of pepsin in the gastric juice; Kühne introduced the name enzymes; Büchner has shown, the presence of zymase in yeast capable of setting up alcoholic fermentation.

Mr. Fairchild considered the different theories in regard to fermentation: the production of digestive ferments by the animal cell their action upon the various kinds of tissues with which they may be brought into contact, and the different conditions and substances which influence and destroy their action. This was then followed by the consideration of the utilization and isolation of these physiological principles, and especially the advances made in bringing them into available form in medicine.

The use of pepsin in medicine and pharmacy was referred to in detail by the speaker, who said that the first pepsin to be prepared in a commercial way was of French origin. The introduction of pepsin into the different Pharmacopœias was discussed, their strengths noted, as also the manner of testing. The different methods for extracting and preparing pepsin for the market were considered, and the author in this connection presented the different theories in regard to the origin of pepsin, the peculiar conditions necessary for the action of digestive ferments, and the care that should be exercised in combining them with substances that either have only an inhibitory effect or destroy their action entirely.

The pancreatic ferments were dealt with, the author discussing their properties, compatibilities, and their use in the artificial digestion of foods. He said that while pancreatic juice is held to be alkaline in character, nevertheless he finds the fresh gland and infusions therefrom to be invariably acid.

In discussing the paper, Dr. Lowe referred to the erroneous notions held by many in regard to the influence that ferments have in digestion. J. W. England moved that a special vote of thanks be tendered to Mr. Fairchild for his valuable paper, and said that it seemed especially appropriate for it to be presented at this time, as it was just thirty years ago that E. Scheffer published a paper in the

AMERICAN JOURNAL OF PHARMACY on the preparation of pepsin (1872, p. 49). The motion was unanimously adopted.

The next paper was on "The Filtration of Drinking Water," by William G. Toplis (see p. 67). The author, in connection with the paper, demonstrated the construction of a sand-filter, and said that in the purification of water no less than three separate and distinct classes of organisms are concerned: the first changing the organic matter into ammonia; a second group changing the ammonia into nitrous acid; and finally, a third forming from the latter nitric acid. He also alluded to the different methods for the biological and chemical examination of water.

A paper on the "Solubility of Compressed Tablets" (see p. 80), by A. M. Hance, was read on behalf of the author by W. C. White. The author said that the term solubility, as applied to tablets, indicates the power to disintegrate rather than power to form solutions.

Rolland H. French presented a paper on "Seidlitz Powders" (see p. 74). The author said that for all commercial purposes the analysis of Seidlitz mixture might be reduced to simply a CO_2 determination, from which the sodium bicarbonate was calculated and the Rochelle salt found by difference.

"Progress in Pharmacy" was the title of an excellent paper (see p. 82) by M. I. Wilbert, Apothecary to the German Hospital. The author briefly reviewed some of the advances made during the past year, and among other things called attention to the fact that the requirements of the German Pharmacopœia are of such a nature that many German apothecaries have found it advisable to attend short post-graduate courses, embracing work with the compound microscope and volumetric analysis.

Owing to lack of time the "Discussion on Modern Drug Store Methods" was postponed until the next meeting.

Among the exhibits was that of Merck & Co., who exhibited a specimen of gaduol (the alcoholic extract of cod-liver oil) and the various preparations which can be made from it, as with hypophosphites, peptonized iron, dionin and thiocol. The exhibit also included thiocol (guaiacol-sulphonate of potassium) and dionin (ethyl-morphine hydrochlorate).

Gilpin, Langdon & Co. exhibited a line of spices; they also had a number of samples for distribution. An exhibition of metal goods, including pill machines, bottle stoppers and collapsible tubes, was made by A. H. Wirz.

The following provisional program has been arranged for the next meeting, February 18th:

"The Basis of Atomic Weights." By Prof. Edgar F. Smith, University of Pennsylvania.

"Adulteration of Drugs and Foods." By Dr. Albert Robin, Delaware State Board of Health.

"Deodorized Opium Preparations." By Albert E. Ebert, Chicago.

"Dose Measures and Measure Doses." By M. I. Wilbert.

"Discussion on Modern Drug-Store Methods." H. K.

PHILADELPHIA COLLEGE OF PHARMACY.

The quarterly meeting of the members of the Philadelphia College of Pharmacy was held December 30, 1901, the President, Howard B. French, in the chair. Twenty-two members were present. The minutes of the semi-annual meeting, held September 30th, were read and approved.

The minutes of the Board of Trustees for the meetings held September 3d, October 1st, and November 6th, were read by the Registrar, W. Nelson Stem, and approved.

Announcement was made of the death of our fellow-member, Charles W. Warrington, which occurred at his residence, 1700 Mount Vernon Street, on November 13th. He became a member in 1900.

A communication was read from Mr. F. W. E. Stedem, resigning his membership in the College—to take effect immediately. All the requirements for resignation having been complied with, it was on motion accepted.

At the semi-annual meeting held September 30, 1901, it was "resolved that a committee of five be appointed to take into consideration all matters pertaining to the meeting of the American Pharmaceutical Association in 1902, in which the College may be interested." The President appointed the committee as follows: H. L. Stiles, Chairman; Mahlon N. Kline, Wm. L. Cliffe, George M. Beringer, and Walter A. Rumsey.

The Committee on Membership presented a communication proposing the names of three persons for election to Honorary Membership.

The Committee further recommends that renewed efforts be made to increase the Associate Membership in the College, calling attention to the privileges conferred on this class of members, which are:

1. The regular receipt of THE AMERICAN JOURNAL OF PHARMACY.
2. Access to Library.
3. All other privileges of membership except that of voting.

A certificate is given to Associate Members, and it seems only necessary for these facts to be presented properly to the students and others for them to become members.

C. A. WEIDEMANN, M.D.,
Secretary.